REPUBLIKA SLOVENIJA
Ministrstvo za gospodarstvo

URAD REPUBLIKE SLOVENIJE ZA INTELEKTUALNO LASTNINO

Potrdilo

Certificate

Urad Republike Slovenije za intelektualno lastnino potrjuje, da je priloženi dokument istoveten z izvirnikom patentne prijave, kot sledi:

Slovenian Intellectual Property Office hereby certifies that the document annexed hereto is a true copy of the patent application, as follows:

(22) Datum prijave (*Application Date*):

21.6.2002 (21.jun.2002)

(21) Številka prijave (*Application No.*):

P-200200160

(54) Naziv (*Title*):

HITRO RAZPADLJIVE TABLETE

Ljubljana, 27.5.2003

Janez Kukec-Mezek
svetovalec Vlade

REPUBLIKA SLOVENIJA MINISTRSTVO ZA GOSPODARSTVO Urad Republike Slovenije za intelektualno lastnino LJUBLJANA 13

REPUBLIKA SLOVENIJA URAD ZA INTELEKTUALNO LASTNINO

REPUBLIKA SLOVENIJA
MINISTRSTVO ZA GOSPODARSTVO

URAD REPUBLIKE SLOVENIJE
ZA INTELEKTUALNO LASTNINO
1000 LJUBLJANA, KOTNIKOVA 6

ZAHTEVA ZA PODELITEV PATENTA

1. Naslov za obveščanje:

Lek d.d.

Verovškova 57

1526 Ljubljana

tel.: 580 23 70
faks: 568 21 23 šifra:MD/

Potrdilo o prejemu prijave
(izpolni urad)

Datum vložitve prijave: 21. 6. 2002

Številka prijave: P-200200160

ig urada in podpis:

2. Prijavitelj (priimek, ime in naslov, za pravne osebe firma in sedež):

Lek, tovarna farmacevtskih in kemičnih izdelkov, d.d.
Verovškova 57
1526 Ljubljana

3. Zastopnik: Registrska številka:

4. Izumitelj (priimek, ime in naslov):

Škulj Vesna , Hafnerjeva ul. 1, 1000 Ljubljana

5. Naziv izuma:

Hitro razpadljive tablete

6. Podatki o zahtevani prednostni pravici in podlagi zanjo:

7. Dodatne zahteve:

- ☐ prijava je za patent s skrajšanim trajanjem
- ☐ predhodna objava patenta po preteku ____ mesecev
- ☐ prijava je izločena iz prijave številka: _____

8. Izjava:

- ☐ izjava o skupnem predstavniku:

9. Priloge:

- ✓ x opis izuma, ki ima _5___ strani 2x
- ✓ x patentni zahtevek (zahtevki), ki ima(jo) __1__ strani; število zahtevkov: _13___ 2x
- ✓ ☐ skice (če so zaradi opisa izuma potrebne); število listov: ____
- x povzetek 2x
- ☐ potrdilo o plačilu prijavne pristojbine
- ☐ potrdilo o deponiranju biološkega materiala, če gre za izum, ki ga ni mogoče drugače opisati
- ☐ pooblastilo zastopniku
- ☐ generalno pooblastilo zastopniku je deponirano pri uradu pod št.: _____
- ☐ potrdilo o razstavni prednostni pravici
- ☐ podatki o drugih prijaviteljih
- ✓ x podatki o drugih izumiteljih
- ☐ prikaz zaporedja nukleotidov ali aminokislin v opisu

REPUBLIKA SLOVENIJA
MINISTRSTVO ZA GOSPODARSTVO

URAD REPUBLIKE SLOVENIJE
ZA INTELEKTUALNO LASTNINO
1000 LJUBLJANA, KOTNIKOVA 6

☑ x prijava je bila predhodno posredovana po faksu ali v elektronski obliki
☐ _____

Lek d.d.
Alenka Košak

_____
Priimek in ime ter podpis prijavitelja (zastopnika

Podatki o drugih izumiteljih:

Širca Judita, Gašperšičeva ul. 7, 1000 Ljubljana

Jenko Osel Maja, Žerjavka 14, 4000 Kranj

Lek, tovarna farmacevtskih in kemičnih izdelkov, d.d.

Hitro razpadljive tablete

Področje izuma

Izum spada v področje farmacevtske tehnologije in se nanaša na hitro razpadljive tablete, ki se lahko uporabljajo kot oralno disperzibilne tablete in kot disperzibilne tablete, ki jih raztopimo v vodi.

Stanje tehnike

V patentih so opisane različne tehnike priprave hitro razpadljivih tablet. Priprava oralno disperzibilnih tablet je običajno tehnološko zelo zahtevna. Pogosto so potrebne posebne, drage naprave. Omenjena tehnologija je primerna le za pripravo oralno disperzibilnih tablet, v katerih je nizka doza učinkovine.

V patentnih prijavah WO 96/21429, WO 97/17947 in WO 99/15155 so opisane običajne farmacevtske oblike, ki vsebujejo mikrokristalno celulozo z vključenim silicijevim dioksidom. Te tablete vsebujejo tudi superdisintegrant, npr. Na kroskarmelozo.

Iz WO 92/19227 so poznane disperzibilne tablete, ki vsebujejo amoksicilin in klavulansko kislino. Izdelane so tako, da najprej kompaktirajo učinkovini skupaj z delom pomožnih snovi. Tako pridobljen granulat nato zmešajo s preostankom pomožnih snovi ter zmes tabletirajo. Kot disintegrant uporabljajo premrežen polivinilpirolidon, Na kroskarmelozo in/ali Na-škrob glikolat. V opisu ni omenjeno, da bi se tablete lahko uporabljale kot oralno disperzibilne tablete.

Opis izuma

Izum se nanaša na hitro razpadljive tablete, ki se lahko uporabljajo kot oralno disperzibilne tablete, ki v ustih razpadejo v manj kot 60 sekundah. Lahko pa se uporabljajo tudi kot disperzibilne tablete, ki jih pred zaužitjem raztopimo v vodi. To smo dosegli z enostavno tehnologijo z uporabo mikrokristalne celuloze z

vključenim silicijevim dioksidom, brez dodatka superdisintegrantov. Tehnologija omogoča pripravo oralno disperzibilnih tablet z visoko dozo učinkovine.

Oblika je pacientu prijazna, posebej primerna za otroke in starejše ljudi ter za tiste, ki imajo težave s požiranjem. Prednost oblike je, da se lahko uporablja tudi v razmerah, kjer pitna voda ni dosegljiva. Oblika je še posebej primerna za antibiotike. Uporablja se lahko tudi v pediatriji za otroke starejše od 3 let.

Tablete po predloženem izumu vsebuje najmanj eno učinkovino, mikrokristalno celulozo z vključenim silicijevim dioksidom, drsljivec ter druge pomožne snovi kot so npr. sladila, arome in barvila.

Učinkovina je izbrana iz skupine antibiotikov, ki obsega beta-laktamske antibiotike iz skupin cefalosporinov in penicilinov (kot so aminopenicilini, npr. amoksicilin ter kombinacija amoksicilina in klavulanske kisline), makrolide, kinolone, aminoglikozide, tetracikline in druge.
Doza učinkovine je lahko zelo različna, odvisna od posamezne učinkovine. Tableta lahko vsebuje do 1500 mg učinkovine. Delež učinkovine v tableti je od 5 do 70 ut. %.
Za pedlatrično uporabo je možno kombinirati tablete različnih jakosti, da lahko dozo prilagodimo otrokovi teži.

Mikrokristalna celuloza z vključenim silicijevim dioksidom je lahko katerakoli komercialno dostopna oblika tega ingredienta, npr. Prosolv SMCC, ki ga proizvaja Penwest Company in je opisan v WO 96/21429. Njen delež v tableti je 30 do 95 %. Razmerje učinkovine in mikrokristalne celuloze z vključenim silicijevim dioksidom je lahko od 0,5 : 1 do 2,5 :1.

Drsljivec je izbran iz skupine hidrofobnih drsljivcev kot so hidrogenirana maščobna olja, Mg stearat, stearinska kislina. Posebno primeren drsljivec je izbran iz skupine hidrogeniranih maščobnih olj. Prednostno je to hidrogenirano ricinusovo olje Cutina HR, Henkel.

Kot sladila se v tabletah uporabljajo umetna sladila kot so npr. aspartam, Na-saharinat, acesulfam K ali pa tudi naravni sladkorji. Arome so lahko izbrane izmed običajnih arom kot so naravne arome, naravno identične arome, umetne arome različnih okusov.

Tablete lahko vsebuje tudi organske kisline npr. citronsko kislino, sušilna sredstva. Učinkovinam s posebno neprijetnim okusom lahko predhodno maskiramo okus.

Postopek priprave tablet, ki so predmet tega izuma, je zelo enostaven. Učinkovino in pomožne snovi zmešamo, zmes homogeniziramo, presejemo in direktno tabletiramo. Predhodno suho ali mokro granuliranje ni potrebno.

Tablete ustrezajo vsem farmakopejskim standardom za tablete, oralno disperzibilne in disperzibilne tablete.

Predmet izuma so tudi hitro razpadljive tablete, ki vsebuje kombinacijo amoksicilina in klavulanske kisline. Lahko se uporabljajo kot oralno disperzibilne tablete in kot disperzibilne tablete. Uporaba mikrokristalne celuloze z vključenim silicijevim dioksidom je omogočila izdelavo oralno disperzibilne tablete z visoko dozo amoksicilina in klavulanske kisline, ki do sedaj ni bila poznana. Tablete lahko vsebujejo 250 - 1500 mg amoksicilina in ustrezno količino klavulanske kisline.

Amoksiciklin je v tableti lahko v obliki trihidrata, klavulanska kislina v obliki soli, prednostno kalijevega klavulanata. Razmerje obeh učinkovin je od 2:1 do 30:1, posebej primerna so razmerja 4:1, 7:1, 8:1, 12:1, 14:1 in 16:1.

Običajno je potrebno pri tabletah, ki vsebujejo amoksicilin in klavulansko kislino, najprej pripraviti granulat iz učinkovin ter dela pomožnih snovi. Granulat se nato zmeša s preostalim delom pomožnih snovi in zmes tabletira.
Tablete, ki so predmet tega izuma pripravimo z direknim tabletiranjem, predhodno granuliranje ali ekstrudiranje ni potrebno. Ker je kalijev klavulanat izredno občutljiv na vlago, je potrebno uporabiti predhodno sušene ingrediente. Delo mora potekati v prostorih, kjer relativna zračna vlaga ne sme presegati 25%.

Posebno maskiranje okusa ni potrebno, dodana so samo običajna sladila in arome. Tablete so prijetnega okusa ter hitro razpadejo v ustih ali v vodi. Fizikalne lastnosti tablet so primerne za pakiranje na običajnih pakirnih linijah, kar pri hitro razpadljivih tabletah, ki so izdelane z drugimi tehnologijami, ni običajno.

Tablete lahko uporabljamo tudi v pediatriji. Ker so prijetnega okusa in se enostavno zaužijejo (raztopijo neposredno v ustih ali v vodi) so primerne za otroke, ki so starejši od 3 let. Odmerjanje je potrebno prilagoditi otrokovi telesni masi in klinični sliki. Pripravimo lahko tablete različnih jakosti, ki jih je možno medsebojno kombinirati s ciljem doseči optimalni odmerek glede na otrokovo telesno maso, klinično sliko in povzročitelja bolezni.

Izum pojasnjujejo in nikakor ne omejujejo naslednji izvedbeni primeri:

Primer 1:

Sestava za 1 tableto:

INGREDIENTI		
Amoksicilin (v obliki trihidrata)	875	mg
Klavulanska kislina (v obliki kalijevega klavulanata)	125	mg
aspartam	9	mg
aroma	36	mg
Aerosil 200	18	mg
Cutina HR	36	mg
smukec	18	mg
Prosolv SMCC 90	do 1932	mg

Postopek izdelave:
Vse ingrediente zmešamo, homogeniziramo, presejemo in direktno tabletiramo.

Primer 2:

Sestava za eno tableto:

INGREDIENTI		
Amoksicilin (v obliki trihidrata)	500	mg
Klavulanska kislina (v obliki kalijevega klavulanata)	125	mg
aspartam	6,5	mg
aroma	26	mg
Aerosil 200	13	mg
Cutina HR	26	mg
smukec	13	mg
Prosolv SMCC 90	do 1300	mg

Primer 3:

Sestava za eno tableto:

INGREDIENTI		
Amoksicilin (v obliki trihidrata)	437,5	mg
Klavulanska kislina (v obliki kalijevega klavulanata)	62,5	mg
aspartam	4,5	mg
aroma	18	mg
Aerosil 200	9	mg
Cutina HR	18	mg
smukec	9	mg
Prosolv SMCC 90	do 966	mg

Primer 4:

Sestava za eno tableto:

INGREDIENTI		
Amoksicilin (v obliki trihidrata)	250	mg
Klavulanska kislina (v obliki kalijevega klavulanata)	62,5	mg
aspartam	3,25	mg
aroma	13	mg
Aerosil 200	6,5	mg
Cutina HR	13	mg
smukec	6,5	mg
Prosolv SMCC 90	do 650	mg

PATENTNI ZAHTEVKI

1. Hitro razpadljiva tableta, ki vsebuje:
   - eno ali več učinkovin
   - mikrokristalno celulozo z vključenim silicijevim dioksidom
   - druge pomožne snovi

2. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da se uporablja kot oralno disperzibilna tableta in kot disperzibilna tableta.

3. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da je učinkovina izbrana izmed antibiotikov.

4. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da vsebuje kombinacijo amoksicilina in klavulanske kisline.

5. Hitro razpadljiva tableta po zahtevkih 1 in 4, označena s tem, da je razmerje amoksicilina in klavulanske kisline od 2:1 do 30:1.

6. Hitro razpadljiva tableta po zahtevkih 1 in 4, označena s tem, da je razmerje amoksicilina in klavulanske kisline 1:4.

7. Hitro razpadljiva tableta po zahtevku 1 in 6, označena s tem, da je razmerje amoksicilina in klavulanske kisline 1:7.

8. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da je delež učinkovine v tableti od 5 do 70 ut. %.

9. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da se kot mikrokristalna celuloza z vključenim silicijevim dioksidom uporablja Prosolv SMCC.

10. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da je razmerje učinkovine in mikrokristalne celuloze z vključenim silicijevim dioksidom od 0,5 : 1 do 2,5 : 1.

11. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da je delež mikrokristalne celuloze z vključenim silicijevim dioksidom 30 do 95 ut. %.

12. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da se kot drsljivec uporablja Cutina HR.

13. Hitro razpadljiva tableta po zahtevku 1, označena s tem, da se uporablja v pedlatriji.

POVZETEK

Izum se nanaša na hitro razpadljive tablete, ki se uporabljajo kot oralno disperzibilne tablete in kot disperzibilne tablete. Zaužijemo jih lahko tako, da jih raztopimo neposredno v ustih ali v vodi. Tablete vsebujejo mikrokristalno celulozo z vključenim silicijevim dioksidom. Posebno primerne so so za antibiotike. Lahko se uporabljajo tudi v pediatriji pri otrocih starejših od treh let. Opisane so tudi oralno disperzibilne tablete, ki vsebujejo amoksicilin in klavulansko kislino.

REPUBLIC OF SLOVENIA

Ministry of Economic Affairs

SLOVENIAN INTELLECTUAL PROPERTY OFFICE

Certificate

Slovenian Intellectual Property Office hereby certifies that the document annexed hereto is a true copy of the patent application, as follows:

(22) Application Date:

21 June 2002

(21) Application No.:

P-200200160

(54) Title:

RAPIDLY DISINTEGRATING TABLETS

Ljubljana, 27 May 2003

Janez Kukec-Mezek
Government Counsellor

L.S.
Republic of Slovenia
Ministry of Economic Affairs
Slovenian Intellectual Property Office
Ljubljana

Kotnikova 6, 1001 Ljubljana, POB 206, telephone: 01/478 3100, fax: 01/478 3111

REPUBLIC OF SLOVENIA
MINISTRY OF SCIENCE AND TECHNOLOGY

SLOVENIAN INTELLECTUAL
PROPERTY OFFICE
1000 LJUBLJANA, Kotnikova 6

REQUEST FOR A PATENT GRANT

1. Address for correspondence:

Lek d.d.
Verovškova 57
1526 Ljubljana

Telephone: 580 23 70
Fax: 568 2123 code: MD/

Acknowledgement of the application
(for official use only)

Date of application receipt:

21 June 2002

Application number:

P-200200160

Stamp and signature:

2. Applicant (Family name followed by given name and address; for a legal entity, full official designation

Lek , Pharmaceutical and Chemical Company d.d.
Verovškova 57
1526 Ljubljana

3. Representative: Registration No.:

4. Inventor (Family name followed by given name and address):

Škulj Vesna, Hafnerjeva ul. 1, 1000 Ljubljana

5. Title of invention:

Rapidly Disintegrating Tablets

6. Claimed priority right:

7. Additional requests:

- ☐ application for a shortened duration patent
- ☐ preliminary publication after the expiry of ___months
- ☐ application is divided from the application no.:___

8. Statements:

- ☐ statement of common representative

REPUBLIC OF SLOVENIA
MINISTRY OF SCIENCE AND TECHNOLOGY

SLOVENIAN INTELLECTUAL
PROPERTY OFFICE
1000 LJUBLJANA, Kotnikova 6

9. Enclosures:

- x Description of the invention, having 5 pages 2x
- x Patent claim (claims), having 1 pages; number of claims: 13 2x
- ☐ Schemes (if required for patent description); number of sheets:
- x Abstract 2x
- ☐ Voucher for the settlement of fees
- ☐ Declaration of depositing the biological material if it is an invention which cannot be described
- ☐ Authorisation to the representative
- ☐ General authorisation to the representative is deposited in the office under no. .....
- ☐ Declaration on priority right
- ☐ Information about additional applicants
- x Information about additional inventors
- ☐ Presentation of nucleotide or amino acid sequence in the description
- ☐ Application was previously faxed or mailed in electronic form
- ☐ _____

Alenka Košak

_____

Applicant's (representative's) family name
followed by given name and signature,

Information about additional inventors:

Širca Judita, Gašperšičeva ul. 7, 1000 Ljubljana

Jenko Osel Maja, Žerjavka 14, 4000 Kranj

Lek Pharmaceutical and Chemical Company, d.d.

Rapidly disintegrating tablets

Field of the invention

The present invention belongs to the field of the pharmaceutical technology and it relates to rapidly disintegrating tablets intended to be used as orodispersible tablets or dispersible tablets which are dispersed in water.

Prior art

Different techniques for preparation of rapidly disintegrating tablets are described in the patents. The preparation of orodispersible tablets is generally technologically very demanding. Special, expensive apparatus are often needed. The said technology is suitable only for preparation of the orodispersible tablets with low dosage of the active substance.

The patent applications WO 96/21429, WO 97/17947 and WO 99/15155 describe the conventional pharmaceutical compositions which include silicified microcrystalline cellulose. These tablets also include a superdisintegrant, e.g., croscarmellose sodium.

Dispersible tablets which contain amoxicillin and clavulanic acid are described in WO 92/19227. These dispersible tablets are prepared as follows: The active substances are first compacted together with a portion of the excipients. The obtained granulate is then mixed with the remainder of the excipients and the resulting mixture is compressed into tablets. The disintegrants used are cross-linked N-vinyl-2-pyrrolidone, croscarmellose sodium and/or sodium starch glycollate. In the description there is no data if the tablets are suitable to be used as orodispersible tablets.

Description of the invention

The present invention relates to the rapidly disintegrating tablets suitable to be used as orodispersible tablets which are disintegrated in the oral cavity in less than 60 seconds. They may also be used as dispersible tablets which are dispersed in water prior to ingestion. We have attained it by simple technology

using silicified microcrystalline cellulose without the addition of superdisintegrants. This technology enables preparation of the orodispersible tablets with high dosage of the active substance.

The pharmaceutical composition is acceptable to patients; particularly it is suitable for children and elderly individuals and for those who have difficulty in swallowing. An advantage of the pharmaceutical composition is that it may be used in circumstances when drinking water is not available. The pharmaceutical composition is especially appropriate for antibiotics. It is also suitable for use in pediatric patients in the age above 3 years.

The tablets of the present invention comprise at least one active substance together with silicified microcrystalline cellulose, a lubricant and other excipients such as, for example, sweetening agents, flavours and colouring agents.

The active substance is selected from the group of antibiotics comprising beta-lactam antibiotics from the groups of cephalosporins and penicillins (such as aminopenicillins, for example, amoxicillin and a combination of amoxicillin and clavulanic acid), macrolides, quinolones, aminoglycosides, tetracyclines and others.
The dose of the active substance could vary depending on an individual active substance. The tablets may contain to 1500 mg of the active substance. The proportion of the active substance in the tablet is from 5 to 70% by weight.
For pediatric use the tablets of different dose strengths may be combined to adjust the dose according to child's body weight.

Silicified microcrystalline cellulose may be any commercially available form of this ingredient, for example, Prosolv SMCC, manufactured by Penwest Company and is described in WO 96/21429. Its proportion in the tablet is 30 to 95 %. A ratio of the active substance and silicified microcrystalline cellulose may be in the range 0.5 : 1 to 2.5 :1.

A lubricant is selected from the group of hydrophobic lubricants such as hydrogenated fatty oils, magnesium stearate, and staeric acid. Especially suitable lubricant is selected from hydrogenated fatty oils. Preferably it is hydrogenated castor oil Cutina HR, Henkel.

Sweetening agents used in the tablets may be artificial sweetening agents such, for example aspartame, saccharin sodium, acesulfame potassium or also natural sugars. Flavouring agents may be selected from conventional favours such as natural flavouring agents, synthetic equivalents identical to natural favouring agents, artificial flavouring agents of different tastes.

The tablets may also include organic acids, for example, citric acid, desiccants. A particularly unpleasant taste of the active substances may be previously masked.

The process for preparation of the tablets of this invention is very simple. The active substance and excipients are mixed; the mixture is homogenized, sieved and directly compressed to tablets. Previous dry or wet granulation is not needed.

The tablets correspond to all pharmacopoeial standards for tables, orodispersible tablets and dispersible tablets.

Rapidly disintregrating tablets which contain a combination of amoxicillin and clavulanic acid are also the object of the present invention. They are suitable for use as orodispersible tablets or dispersible tablets. The use of silicified microcrystalline cellulose has enabled manufacture of orodispersible tablets with high dosage of amoxicillin and clavulanic acid, insofar being unknown. The tablets may contain 250 to 1500 mg of amoxicillin and the appropriate quantity of clavulanic acid.

Amoxicillin in the tablet may be in the form of trihydrate, clavulanic acid in the form of the salt, preferably potassium clavulanata. The ratio of the two active substances is 2:1 to 30:1, especially suitable are the ratios 4:1, 7:1, 8:1, 12:1, 14:1 and 16:1.

For the tablets containing amoxicillin and clavulanic acid, it is generally necessary to prepare first the granulate comprising the active substances and a part of the excipients. The granulate is then mixed with the remaining part of the excipients, and the mixture is compressed to tablets
The tablets of the present invention are prepared by direct compressing into tablets, previous granulation or extrusion is not necessary. As potassium clavulanate is highly moisture sensitive, previously dried ingredients should be used. Work should be carried out under conditions of relative humidity not exceeding 25%.

Special masking of the taste is not necessary, only common sweeteners and flavours are added. The tablets are of the pleasant taste and are dispersed rapidly in the mouth or in water. The physical characteristics of the tablets are suitable for packaging on a conventional packaging line which with rapidly disintegrating tablets manufactured by other technologies is not conventional.

The tablets are also suitable for use in pediatric patients. Since they are of the pleasant taste and administered in the simple way (dispersed in the mouth or in water) they are suitable for children above 3 years of age. The dosage should be adjusted according to child's body weight, and clinical picture. The tablets of the different strengths can be formulated which may be combined aimed at attaining the optimal dosage regarding the child's body weight, clinical picture and infective causative agent.

The present invention is illustrated but in no way limited by the following examples:

Example 1:

Composition of one tablet:

INGREDIENTS	
Amoxicillin (in the form of trihydrate)	875 mg
Clavulanic acid (in the form of potassium clavulanate)	125 mg
Aspartama	9 mg
Flavour	36 mg
Aerosil 200	18 mg
Cutina HR	36 mg
Talc	18 mg
Prosolv SMCC 90	to 1932 mg

The method of manufacture:
All ingredients are mixed, homogenized, sieved and compressed directly into tablets.

Example 2:

Composition of one tablet:

INGREDIENTI	
Amoxicillin (in the form of trihydrate)	500 mg
Clavulanic acid (in the form of potassium clavulanate)	125 mg
Aspartama	6.5 mg
Flavour	26 mg
Aerosil 200	13 mg
Cutina HR	26 mg
Talc	13 mg
Prosolv SMCC 90	to 1300 mg

Example 3:

Composition of one tablet:

INGREDIENTI	
Amoxicillin (in the form of trihydrate)	437.5 mg
Clavulanic acid (in the form of potassium clavulanate)	62.5 mg
Aspartama	4.5 mg
Flavour	18 mg
Aerosil 200	9 mg
Cutina HR	18 mg
Talc	9 mg
Prosolv SMCC 90	to 966 mg

Example 4:

Composition of one tablet:

INGREDIENTI	
Amoxicillin (in the form of trihydrate)	250 mg
Clavulanic acid (in the form of potassium clavulanate)	62.5 mg
Aspartama	3.25 mg
Flavour	13 mg
Aerosil 200	6.5 mg
Cutina HR	13 mg
Talc	6.5 mg
Prosolv SMCC 90	to 650 mg

CLAIMS

1. A rapidly disintegrating tablet comprising:
   - one or more active substances
   - silicified microcrystalline cellulose
   - other excipients

2. The rapidly disintegrating tablet according to claim 1 intended to be used as orodispersible tablet or dispersible tablet.

3. The rapidly disintegrating tablet according to claim 1 wherein the active substance is selected from the antibiotics.

4. The rapidly disintegrating tablet according to claim 1 wherein the active substance is the combination of amoxicillin and clavulanic acid.

5. The rapidly disintegrating tablet according to claims 1 and 4 wherein the ratio of amoxicillin to clavulanic acid is in the range of 2 :1 to 30 :1.

6. The rapidly disintegrating tablet according to claims 1 and 4 wherein the ratio of amoxicillin to clavulanic acid is 4 :1.

7. The rapidly disintegrating tablet according to claims 1 and 6 wherein the ratio of amoxicillin to clavulanic acid is 7 :1.

8. The rapidly disintegrating tablet according to claim 1 wherein the proportion of the active substance in the tablet is 5 to 70 % by weight.

9. The rapidly disintegrating tablet according to claim 1 wherein the silicified microcrystalline cellulose is Prosolv SMCC.

10. The rapidly disintegrating tablet according to claim 1 wherein the ratio of the active substance and silicified microcrystalline cellulose is 0.5 : 1 to 2.5 : 1.

11. The rapidly disintegrating tablet according to claim 1 wherein the proportion of silicified microcrystalline cellulose is 30 to 95% by weight.

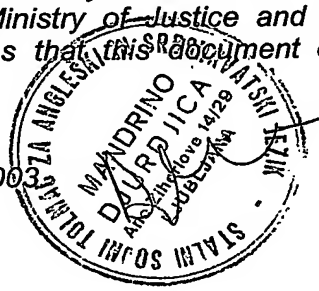
12. The rapidly disintegrating tablet according to claim 1 wherein the lubricant is Cutina HR.

13. The rapidly disintegrating tablet according to claim 1 characterized in that it is suitable for the use in pediatric patients.

ABSTRACT

The present invention relates to rapidly disintegrating tablets intended to be used as orodispersible tablets or dispersible tablets. They are ingested either by dispersing directly in the mouth or in water. The tablets include silicified microcrystalline cellulose. They are especially suitable for antibiotics. These tablets are also suitable for use in pediatric patients in the age above 3 years. Orodispersible tablets which contain amoxicillin and clavulanic acid are also described.

The undersigned Djurdjica Mandrino, permanent court interpreter for the English language, appointed by Decree No. 756-4/91, issued on 11th of February 1991 by the Ministry of Justice and Administration, Republic of Slovenia, hereby declares that this document entirely corresponds to the original Slovene text.



Ljubljana, 24 October 2003